UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/913,351	08/13/2001	Aurora Brieva Delgado	B-4275PCT 618999-1	8629

7590 04/29/2004

Richard P Berg
Ladas & Parry
Suite 2100
5670 Wilshire Boulevard
Los Angeles, CA 90036-5679

EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 04/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/913,351	DELGADO ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-10 are pending.

Applicants' response filed January 26, 2004 is acknowledged, and applicants' response has been fully considered. Claims 1-10 are examined.

Informalities

2. The disclosure is objected to because of the following informalities:

The specification cites amino acid sequences at pages 25 and 29, however, no "SEQ ID NO:" is given. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-10 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a non-covalent complex of a polysaccharide and a polypeptide, wherein the polysaccharide has a defined structure (e.g., MW 150 kDa, one phosphate per 15 monosacchrides, known content of mannose, glucose and galactose), and the polypeptide has a minor subunit of SEQ ID NO:2 or 4 and a major subunit of SEQ ID NO:3 or 5 with a MW of 11 or 12 kDa, and wherein the molar ratio of the polysaccharide to the polypeptide is about 1: 2.5, does not reasonably provide enablement for a non-covalent glycoconjugate of a polysaccharide and a polypeptide, where the structure of polysaccharide, the sequence of the polypeptide comprising SEQ ID NO:1 (e.g., only 15 out of 230 amino acids are defined) and the

molar ratio of the polysaccharide to the polypeptide are not defined. The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-10 are directed to a non-covalent glycoconjugate of a polysaccharide and a polypeptide, wherein the polysaccharide has a MW of 50-250 kDa, 1 phosphate per 5-25 monosaccharides, 40% mannose and 60% of glucose and galactose, and wherein the polypeptide comprises SEQ ID NO:1, or is a dimer with a minor subunit of SEQ ID NO:2 or 4 and a major subunit of SEQ ID NO:3 or 5. The specification, however, only discloses cursory conclusions (page 14) without data supporting the findings, which state that the invention describes the formation of non-covalent conjugates of specific polysacchrides and specific polypeptides for manufacturing therapeutic compositions for the treatment of immunological dysfunction, and the conjugates are pharmaceutically active, while none of the components show the pharmaceutical activity of the conjugates. There are no indicia that the present application enables the full scope in view of a non-covalent glycoconjugate of a polysaccharide and a polypeptide as discussed in the stated rejection. The present application does not provide sufficient teachings as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the presence or absence of working examples, the state of the prior art and relative skill of those in the art, the predictability or unpredictability of the art, the nature of the invention, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding the polysaccharides and polypeptides in the non-covalent glycoconjugates, and the effects of the glycoconjugates, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

There are no working examples indicating the claimed variants in the glycoconjugates except for a non-covalent glycoconjugate of a polysacchride and a polypeptide, wherein the polysacchride is isolated from *candida utilis* cells, and the polypeptide is isolated from *Ricinus communis* seeds having a minor subunit of SEQ ID NO:2 or 4 and a major subunit of SEQ ID NO:3 or 5, and wherein the molar ratio of the polysacchride and the polypeptide is about 1:2.5 (Examples 1-3) . The specification has not shown how to make/use glycoconjugates containing various polysacchrides and various polypeptides with different molar ratios.

(3). The state of the prior art and relative skill of those in the art:

The specification indicates polysacchride-protein conjugates with immunomodulatory activities have been described in the prior art, but these conjugates are covalently bonded and come from the same natural source (pages 13-14), while the present invention is directed to non-covalent polysacchride-protein conjugate. Because the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on how to make/use non-covalent glycoconjugate using various polysacchrides and polypeptides of SEQ ID NO:1 with different molar ratios and on the effects of glycoconjugates to be considered enabling for the claimed variant.

(4). Predictability or unpredictability of the art:

The specification has shown that the biological activity of a specific glycoconjugate of a polysacchride isolated from *candida utilis* cells and a polypeptide having a minor subunit of SEQ ID NO:2 or 4 and a major subunit of SEQ ID NO:3 or 5 with the molar ratio of the polysacchride and the polypeptide of 1:2.5 (pages 33-36). Since the pharmacological activities of the glycoconjugate are dependent on the stoichiometries of the two components, polysaccharide and polypeptide (page 14, 4th paragraph of the specification), and the specification has not demonstrated the preparation and pharmacological activities of glycoconjugates containing various polysacchrides and polypeptides of SEQ ID NO:1 with different molar ratios, the effects of various glycoconjugates in inhibiting the production of TNF are unpredictable if the ratio of two components in the glycoconjugates are not specified.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a non-covalent glycoconjugate of a polysaccharide and a polypeptide, wherein the polysaccharide has a MW of 50-250 kDa, 1 phosphate per 5-25 monosaccharides, 40% mannose and 60% of glucose and galactose, and wherein the polypeptide comprises SEQ ID NO:1. The specification indicates the polysaccharide must comply with certain requirements such as MW in the range of 50-250 kDa, 1 phosphate per 5-25 monosaccharides, having at least 40% mannose, the others being glucose and galactose; the polypeptide must have the consensus sequence of SEQ ID NO:1; and the polysaccharide/polypeptide conjugates can be within 1/1 to 1/19 mol/mol range (pages 14-19). However, the specification has not demonstrated the make and use of the glycoconjugates containing various structures of polysaccharides and various sequences of SEQ ID NO:1 with

different molar ratios of the two components. There is no working example indicating the effects of various glycoconjugates except for the glycoconjugate of the polysacchride isolated from *Candida utilis* cells and the polypeptide having a minor subunit of SEQ ID NO:2 or 4 and a major subunit of SEQ ID NO:3 or 5, with the molar ratio of 1:2.5 (Examples 1-3, pages 33-36). Since the specification fails to provide sufficient teachings on the make of various glycoconjugates, nor demonstrates their biological activities, it is necessary to carry out further experimentation to assess the effects of various glycoconjugates.

(6). Nature of the Invention

The scope of the claims encompasses numerous non-covalent glycoconjugates containing a polysaccharide and a polypeptide, but the specification does not provide sufficient teachings on the make/use of various glycoconjugates. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, the working example does not demonstrate the claimed variants, the effects of various glycoconjugates are unpredictable, and the teachings in the specification are limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the effects of various non-covalent glycoconjugates.

In response, applicant indicates the originally filed application provides sufficient information to a person with ordinary skill in the art to enable that person to make and use the claimed invention (page 2 of the response). The response has been fully considered, however, the argument is not found persuasive because the claims encompass numerous structural variants, while the specification has not provided sufficient teachings on the identities and the amounts of various polypeptides and polysacchrides in the glycoconjugate non-covalent

complex, nor has demonstrated the effects of various glycoconjugates, thus a person with ordinary skill in the art to would not be able to make and use the claimed invention as indicated in the section above.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 5 and 8 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5 and 8 are indefinite because of the use of the term "to treat disorders of an immunological system related to a higher production of tumor necrosis factor (TNF)". The term "to treat disorders of an immunological system related to a higher production of tumor necrosis factor (TNF)" renders the claim indefinite, it is unclear what immunological disorders related to higher production of TNF are treated, and what reference point is used for comparison as to "higher production of TNF".

In response, applicants indicate claims 5 and 8 are believed to be sufficient clear to a person with ordinary skill in the art in accordance to the requirements of 35 U.S.C. 112, second paragraph (page 2 of the response). The response has been considered, however, the argument is not found persuasive because the claim does not identify the immunological disorders to be treated, nor indicates the reference point for "higher production of TNF", thus it is not clear what immunological disorders are treated with the claimed glycoconjugates.

Conclusion

5. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Chih-Min Kam, Ph. D. CMK
Patent Examiner

***
April 21, 2004